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a DNA-dependent RNA polymerase II promoter operably linked to a nucleic acid molecule that encodes an antigen from a pathogenic agent.

Attached hereto is a **version showing changes made to claims** and a **currently pending claim set.**

II. REMARKS

Claims 26, 28-31 and 33-44 are pending and stand rejected under 35 U.S.C. § 103. Claim 26 has been amended herein to indicate that the RNA Pol II promoter is DNA-dependent as described throughout the specification. The claim has also been re-formatted into separate paragraphs for improved clarity. No new matter has been added a result of this amendment and entry thereof is respectfully requested. As can be seen by the nature of the amendment, it is also noted that this amendment is made for reasons unrelated to patentability.

In view of the foregoing amendment and following remarks, Applicants request reconsideration of the application and claims.

Rejections Under 35 U.S.C. 103(a)

All of the pending claims stand rejected as allegedly obvious over U.S. Patent No. 6,015,686 (hereinafter "Dubensky"); Polo et al. (hereinafter "Polo") and Cella et al. (hereinafter "Cella").

The Examiner maintains that a *prima facie* case of obviousness has been established and that it is not based upon hindsight reconstruction. See, Page 3 of the Office Action, citing *In re McLaughlin*. The Examiner further maintains that the motivation to combine the references (along with the reasonable expectation of success) is established by the knowledge generally available to one of ordinary skill in the art. (See, Office Action, page 4). Dubensky is alleged to explicitly teach all the elements of

claim 26 "except for expressing a dsRNA in the vector system to induce the production of interferon, which is the first part of claim 26." (Office Action, page 5). Nonetheless, the Examiner asserts that the motivation to combine the references is found in Polo or Cella, which allegedly demonstrate the knowledge generally available to one of ordinary skill in the art. (Office Action, page 5). Finally, it is alleged that the difference between Dubensky's DNA-dependent RNA Pol II promoter and the claimed RNA-dependent promoter is not relevant because it is not claimed. (Office Action, page 7). Even if it were claimed, it is maintained that "it would be obvious to the skilled artisan at the time the invention was made to select the RNA Pol II promoter that is most appropriate for the given application." (Office Action, page 7).

Because the rejection is legally improper and factually flawed, Applicants traverse.

The Office's position is that the knowledge generally available to one of ordinary skill in the art and specific teachings of the art provide the necessary motivation to arrive at the claimed invention. (Office Action, page 4). However, Applicants again note that there are absolutely no teachings in the references that provide the motivation to arrive at an expression cassette comprising two promoters in which one promoter is operably linked to a nucleic acid molecule which, when transcribed *in vivo* forms a double stranded RNA that induces the production of interferon. Indeed, the secondary references, which are relied upon the Examiner as allegedly establishing, in part, the motivation to combine, are completely silent as to expression constructs having two promoters, wherein the promoter operably linked to the nucleic acid molecule encoding an antigen is an RNA polymerase II promoter.

With regard to the alleged general knowledge available at the time of filing, Applicants submit that the Office cannot simply state that the general level of skill in the art was high and, accordingly, the motivation is present. *See, e.g., In re Rouffet,* 47 USPQ2d 1453 (Fed. Cir. 1998) noting that the Office cannot rely on a high level of skill

in the art to overcome the differences between the selected elements in the references, it cannot rely on a high level of skill in the art to provide the necessary motivation. Similarly, in *In re Lee,* 61 USPQ2d 1430 (Fed. Cir. 2002), the Federal Circuit affirmed that common knowledge and common sense are not the specialized knowledge and expertise necessary to establish a motivation to arrive at the claimed invention.

The Office's reliance on *In re McLaughlin*, 170 USPQ 209 (CCPA 1971) is similarly misplaced. *McLaughlin* in no way held that common knowledge are a substitute for evidence, for example as required by 37 C.F.R. 1.104(d)(2). Nor does *McLaughlin*, after 31 years, outweigh the many Federal Circuit and CCPA decisions that the prior art as a whole must suggest the desirability of the making the claimed combination. Virtually all inventions are combinations of old elements. *See, e.g., In re Rouffet,* 47 USPQ2d at 1457. Thus, the requirement is not whether each claimed element can be identified individually in a reference but, rather, whether the Examiner can show "reasons that the skilled artisan, confronted with the same problem as the inventor, and with no knowledge of the claimed invention, would select the elements from the cited prior art reference for combination in the manner claimed." *In re Rouffet,* 47 USPQ2d at 1458. In the pending case, the Office has not shown, with evidence, such reasons and, accordingly, has not established a *prima facie* case of obviousness.

Applicants also address the Office's contention that the difference between Dubensky's RNA-dependent RNA Pol II promoter and the claimed DNA-dependent RNA Pol II promoter is neither a claimed element nor relevant. For clarity, claim 26 has been amended to include this limitation which clearly and unambiguously distinguishes the claimed invention from Dubensky. However, Applicants also note that this difference is entirely relevant because the modifications suggested by the Examiner would destroy the intended function of Dubensky molecule. The law governing obviousness rejections is well-settled -- if the Office's efforts to attain the claimed invention cause the reference to become inoperable or destroy its intended function, then the requisite motivation to

make the modification would not have existed. *See, e.g., In re Fritch*, 23 USPQ2d 1780, 1783 n.12 (Fed. Cir. 1992); *In re Gordon* 221 USPQ 1125, 1127 (Fed. Cir. 1984). In the pending case, the Examiner maintains that it would have been obvious to the skilled artisan at the time the invention was made to select the RNA Pol II promoter that is most appropriate for a given application. See, Office Action, page 7. However, Applicants submit that, in addition to the fact that Dubensky provides no such motivation, Dubensky's ELVIS constructs would not function if the claimed DNA-dependent RNA Pol II promoters were substituted for Dubensky's RNA-dependent Pol II promoters.

Thus, there is no motivation to combine the references as suggested by the Office and, indeed, such a modification would not result in the precisely claimed invention. Moreover, contrary to the Office's assertion there is no reasonable expectation that the claimed invention would be successful. Accordingly, Applicants request that this rejection be withdrawn.

III. CONCLUSION

In view of the foregoing, Applicants submit that the claims are now in condition for allowance and requests early notification to that effect.

Please direct all further communications regarding this application to:

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

26. (Twice Amended) An expression cassette comprising

a promoter operably linked to a nucleic acid molecule which, when transcribed *in vivo*, forms double stranded RNA that induces the production of interferon, and

[an] a DNA-dependent RNA polymerase II promoter operably linked to a nucleic acid molecule that encodes an antigen from a pathogenic agent.

CURRENT PENDING CLAIMS

26. (Twice Amended) An expression cassette comprising

a promoter operably linked to a nucleic acid molecule which, when transcribed *in vivo*, forms double stranded RNA that induces the production of interferon, and

a DNA-dependent RNA polymerase II promoter operably linked to a nucleic acid molecule that encodes an antigen from a pathogenic agent.

28. The expression cassette according to claim 26 wherein said antigen is a viral antigen.

29. The expression cassette according to claim 28 wherein said viral antigen is selected from the group consisting of HIV, HSV, HBV, HCV, HPV, and FIV.

30. The expression cassette according to claim 26 wherein said pathogenic agent is a bacteria, parasite or fungus.

31. The expression cassette according to claim 26 wherein said pathogenic agent is a tumor.

33. The expression cassette according to claim 26 wherein said pol II promoter is selected from the group consisting of CMV, SV40, MoMLV LTR and RSV LTR.

34. A gene delivery vector, comprising an expression cassette according to claim 26.

35. The gene delivery vector according to claim 34 where said vector is a plasmid.

36. The gene delivery vector according to claim 34 where said vector is a recombinant retrovirus.

37. The gene delivery vector according to claim 34 where said vector is a recombinant herpesvirus.

38. The gene delivery vector according to claim 34 where said vector is a recombinant poxvirus.

39. The gene delivery vector according to claim 34 where said vector is a recombinant adenovirus.

40. The gene delivery vector according to claim 34 where said vector is a recombinant parvovirus.

41. The gene delivery vector according to claim 34 where said vector is a recombinant alphavirus.

42. The gene delivery vector according to claim 34 where said vector is a recombinant polyoma virus.

43. (Amended) The gene delivery vector according to claim 34 where said vector is a eukaryotic layered vector initiation system vector.

44. A cell which contains a gene delivery vector according to claim 34.